Biodegradable Fe(II)/Fe(III)-coordination-driven nanoassemblies for chemo/photothermal/chemodynamic synergistic therapy of bacterial infection

Xiaomei Dai*, Yu Li, Xiaojun Liu, Zhangyi Lei, Lele Yang, Qingqing Xu, Feng Gao*

Laboratory of Functionalized Molecular Solids, Ministry of Education, Anhui Key Laboratory of Chemo/Biosensing, Laboratory of Biosensing and Bioimaging (LOBAB), College of Chemistry and Materials Science, Anhui Normal University, Wuhu 241002, P. R. China.

Email: daixiaomei@mail.ahnu.edu.cn

Email: fgao@mail.ahnu.edu.cn

Materials

All reagents were gained by commercial suppliers. *N*-vinyl-2-pyrrolidone (NVP) was purchased from Aladdin (Shanghai, China) and purified by column chromatography prior to use.

Synthesis of (3-Phenylprop-2-ene-1,1-diyl)bis(oxy)bis(ethnane-2,1-diyl)diacrylate (CAE)

CAE was synthesized as previous reported with minor modification.[1] Hydroquinone (1.0 g) and 2-hydroxyl ethyl acrylate (96 mmol) were added in dry benzene at 50 ^{o}C. P-toluenesulfonic acid (0.15 mmol) and cinnamaldehyde (32 mmol) were mixed with the above solution and reacted at 92 ^{o}C for 12 h. Triethylamine was added to quench the reaction after cooling the solution to room temperature. CAE was gained from column chromatography using a solution of ethyl acetate:hexane (2:8) and confirmed by ^{1}H NMR. ^{1}H NMR in $CDCl_3$ on a 400 MHz spectrometer: 3.76 ppm (m, 4H), 3.87 ppm (m, 4H), 5.24 ppm (d, 2H), 5.82 ppm (d, 2H), 6.15 ppm (m, 4H), 6.41 ppm (t, 1H), 7.22-7.41 ppm (m, 5H).

Synthesis of Poly(NVP-*co*-CAE)

NVP (500 μL) was dissolved in 10 mL of DMF, followed by mixing with CAE (100 μL) and 20 mg of AIBN. The mixture was degassed by bubbling argon for 20 min and was immersed in an oil bath preheated to 70 ^{o}C for 12 h. The product was obtained by pouring the mixture into diethyl ether. The molecular weight of poly(NVP-*co*-CAE) was recorded by gel permeation chromatography (GPC, Waters 2690D Separations Module) analysis.

Selective Interaction between bacteria and mammalian cells

NIH 3T3 cells were seeded in the laser confocal dish and cultured at 37 ^{o}C for 24 h. Then, the culture medium was replaced with the fresh medium without antibiotic. Bacterial suspensions (20 μL) were added to the laser confocal. After being incubated for further 30 min, all samples were washed with PBS and stained with hoechest.

Then, all samples were observed by CLSM.

CA release investigation in vitro

The release of CA from the nanoassemblies was evaluated in vitro by dispersing the P2/GA-Fe in PBS at pH 6.0 and 7.4. At the predetermined intervals, the sample were collected, and the release of CA was determined using high performance liquid chromatography.

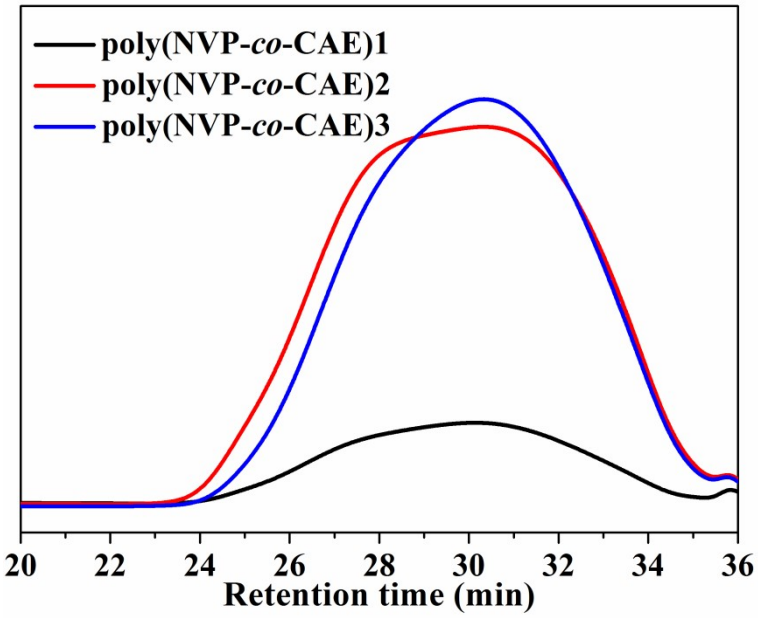

Fig. S1. GPC spectra of poly(NVP-*co*-CAE).

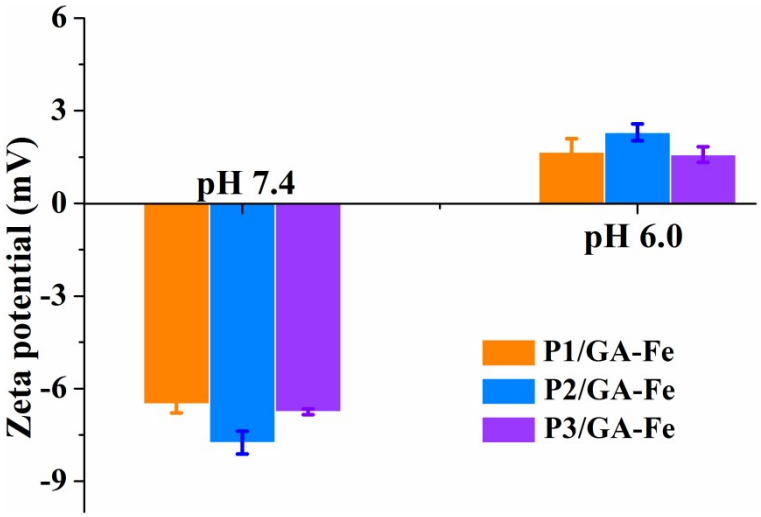

Fig. S2 Zeta potential of P/GA-Fe at pH 7.4 and pH 6.0.

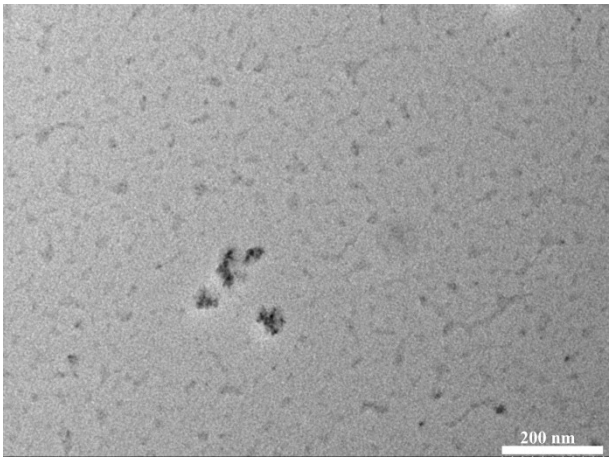

Fig. S3 TEM image of P2/GA-Fe in acid environment for 24 h.

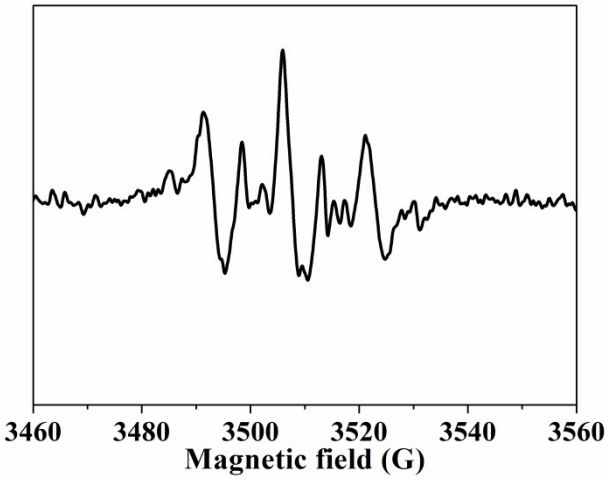

Fig. S4 Electronic paramagnetic resonance test of ROS.

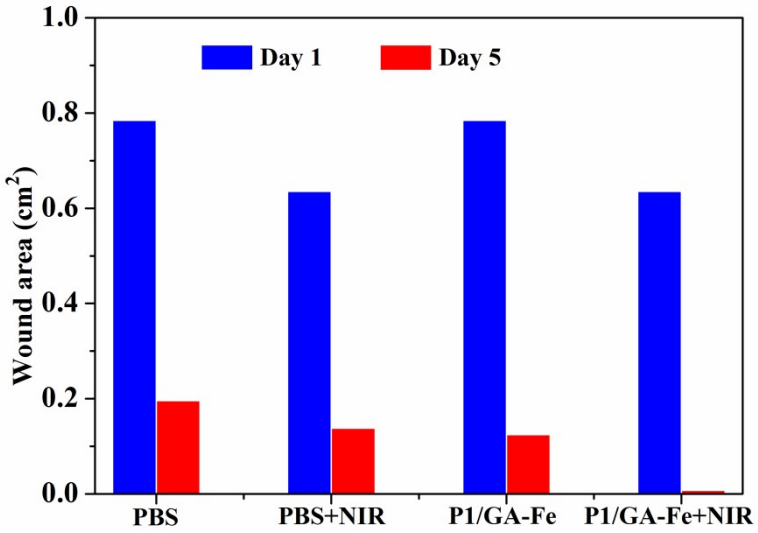

Fig. S5 Wound areas after various treatments.

References

[1] B. Kim, E. Lee, Y. Kim, S. Park, G. Khang and D. Lee, Dual acid-responsive micelle-forming anticancer polymers as new anticancer therapeutics, *Adv. Funct. Mater.* 2013, **23**, 5091-5097.